

The complexity of pain in inflammatory arthropathies beyond pain intensity and impact: An OMERACT initiative

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ABSTRACT

Introduction: People with IA may suffer from pain of differing aetiologies and subtypes including nociceptive joint pain, neuropathic pain of carpal tunnel syndrome or nociplastic pain from concomitant fibromyalgia. Lack of precise measurement tools to identify nociplastic pain influences as a contextual factor potentially all outcomes in collected clinical trials as residual pain might impact various measurements in IA. The OMERACT 2025 pain SIG discussed, developing a scoping review from protocol, to identify an instrument to measure nociplastic pain in IA and a contextualised domain definition for nociplastic pain in IA. Stakeholder opinions were sought regarding pain in IA and the importance of identifying an instrument to measure nociplastic pain in IA.

Methods: A total of twenty-four participants attending the OMERACT 2025 pain SIG session included a mix of patients, clinicians, researchers, methodologists, and industry representatives. Patient research partner (PRP), MC spoke about the impact of pain including different pain subtypes in IA. She recapped the results of OMERACT 2023 poll where participants, including PRPs, agreed that assessing different pain subtypes in IA was important to improve targeted treatments for pain. SK – a pain specialist- presented evidence supporting the presence and impact of nociplastic pain in different IA's including rheumatoid arthritis (RA), psoriatic arthritis (PsA) and axial spondylarthritis (AxSpA). Details of the scoping review protocol developed by the OMERACT Pain Working Group identifying candidate instruments for nociplastic pain assessment in IA was presented. Participants opinions were polled regarding their perspectives of the nociplastic pain definition and measurement.

Results: Polling showed clear agreement on advancing efforts to identify or develop an outcome measure for nociplastic pain. Most participants (86 %, 19/24) endorsed beginning with a systematic review of the existing literature to identify an appropriate validated instrument. Following a pain neuroscience education session five of the six (83 %) patient research partners (PRP) agreed they would be able to report the different pain types experienced in IA. Only one participant (1/24) agreed that the current IASP nociplastic pain definition is directly applicable to IA. Most participants (96 %) either disagreed or were uncertain, and over half (14/24) felt the definition likely requires contextualisation for IA.

Discussion: There was broad agreement that, in a substantial proportion of patients with inflammatory arthritis, nociplastic pain persists despite optimal treatment, is challenging to manage in routine clinical practice, and is associated with substantial patient suffering. The OMERACT meeting underscored the need for a standardized measure of nociplastic pain in inflammatory arthritis to refine eligibility criteria and support the development of stratified approaches in future clinical trials.

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Introduction

Outcome Measures in Rheumatology (OMERACT) is a global multi-disciplinary volunteer-driven organisation committed to improving outcomes for patients with autoimmune musculoskeletal diseases through advancing the design and quality of clinical studies. The OMERACT Pain Working Group focuses on assessing and developing pain outcome measures for rheumatic and musculoskeletal diseases (RMDs). Previous research supports the use of pain intensity and pain impact measures as well-defined domains in clinical studies of inflammatory arthropathies (IA) [1]. Among patient demographics, pain phenotype is an important contextual factor in trials of RMDs, influencing endpoints through effect modification and potentially confounding cohort studies or distorting measurement property findings [2]; therefore, accurate measurement tools applicable for eligibility assessment or risk stratification are essential.

Pain in IA tends to be of mixed pain aetiologies presenting as inflammatory and/or non-inflammatory pain. Inflammatory pain arises from inflamed joints and other musculoskeletal tissue including muscles, tendon and bone while the non-inflammatory pain tends to be associated not only with musculoskeletal inflammation but is also more widespread and recognised as concomitant fibromyalgia (Fig. 1) [3]. Recognising specific pain subtypes is important and the currently used measures of pain intensity or pain impact are unable to provide this information. The OMERACT 2023 pain workshop report [4] suggests mixed pain aetiologies differentially influence disease activity assessment and therapeutic decision-making. Coexisting pain subtypes in IA further impacts the development of suitable outcome measurements and therapeutic strategies. Implementing a mechanism-based approach to pain management may result in improved clinical outcomes, although identifying the exact underlying mechanisms could prove challenging [5].

In 2017 the International Association for the Study of Pain (IASP) introduced the term nociplastic pain [9] which is defined as pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain. Its definition encompasses the non-inflammatory pain of IA and describes pain that is mainly driven by a functional reorganisation of the central nervous system (CNS) rather than inflamed joints or compromised nerves, although peripheral sensitisation also plays a role [8,10,11]. Nociplastic pain may provide some explanations for unexplained chronic musculoskeletal pain that occurs with no clear

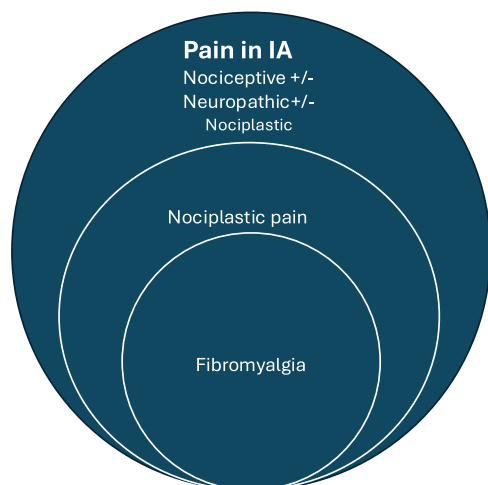


Fig. 1. An Onion diagram representation of pain in IA: Pain in PsA [6,7] and other IA tends to be largely inflammatory but also includes some neuropathic like symptoms and appears to generally fit the defined criteria for Nociplastic pain [8]. This includes a significantly larger cohort of patients with complaints of widespread pain within which lies a smaller cohort of concomitant FM.

evidence of tissue damage or pathology (Box 1 Nociplastic pain definition and criteria). Recognising nociplastic pain in IA may prove challenging to clinicians due to the lack of clear peripheral pathology causing diagnostic ambiguity and ineffective pain management. No single validated instrument can capture all aspects of the nociplastic pain definition and criteria [8]. Therefore, the development of suitable outcome measures and therapeutic strategies for nociplastic pain will improve future clinical outcomes in IA.

The aim of the OMERACT Pain Working Group interactive session was to move beyond the previously discussed complexities of pain in IA [4] and address the specific issue of mechanistic pain types reported in these conditions. Objectives included identifying the need for validated instruments to measure such pain phenotypes, reviewing the development of a scoping literature review of existing instruments capable of measuring nociplastic pain in IA and exploring how nociplastic pain definition and criteria may be applied in the context of IA and further considered as the OMERACT domain definition.

Methods

Setting

OMERACT 2025 was held in Terrassa, Barcelona, Spain, from May 14–17, 2025, and included a wide range of plenary presentations, workshops, and interactive special interest group sessions on outcome measurements in rheumatology.

Special interest group session

During OMERACT 2025, patient and public involvement representative MC Pain PRP introduced the Pain Special Interest Group (SIG) session and outlined the background for the Pain Working Group's proposed scoping review.

SK – a pain specialist – presented up-to-date information regarding the mechanistic pain definition for nociplastic pain and its relevance to pain in IA (Box 1). She also presented the scoping review protocol developed by the OMERACT Chronic Pain Working Group and a preliminary screening of published instruments [12]. During the meeting, it was emphasized that no single instrument fully fulfils the criteria defined for nociplastic pain as defined by IASP [8]. The update on pain of IA included the IASP revised definitions for pain [13] and the various pain subtypes including nociplastic pain definition and its proposed grading criteria [11,8] along with the rationale for conducting a scoping review of outcome measures assessing nociplastic pain in IA [14–16].

Highlights of the scoping review protocol published on the Open Science Framework website [17] and registered on the COMET initiative [18] were presented. A facilitated critical discussion of the definition and diagnostic criteria for nociplastic pain as applied to inflammatory arthropathies was conducted by the pain SIG attendees.

Pain data presented from the 1823 PsA patients in the CorEvitas registry [7] showed that fibromyalgia [19] affected about 1 in 10 patients and widespread pain about 1 in 5 (Fig. 1), both significantly impairing single and composite disease activity measures containing subjective components [2,3] and highlight the confounding impact on cohort study results.

Kosek 2021 published clinical criteria for identifying and grading nociplastic pain in musculoskeletal conditions [8]. Many patients with IA fulfil these criteria [Box 1] and exhibit central sensitisation, reflected by reduced pressure pain thresholds [20] representing static mechanical allodynia or evoked pain hypersensitivity. Concomitant fibromyalgia affecting 4–25 % of patients with PsA and AxSpA, adversely impacting disease activity, mood, fatigue, and sleep [6]. Pain sensitivity and neuropathic-like pain seen in IA serve as an important marker of disease severity, functional disability, and quality of life. Outcome measures of pain sensitivity such the Central Sensitization Inventory reported increased pain sensitivity in 31 % of IA patients as compared to 4.2 % in

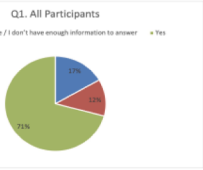
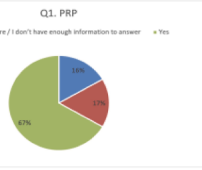
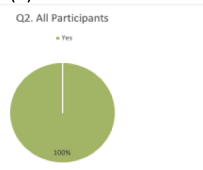
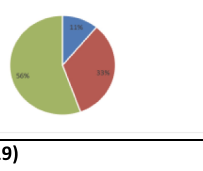
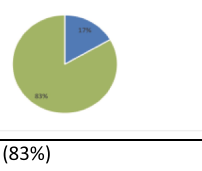
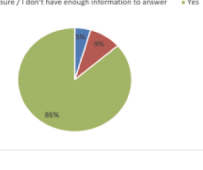
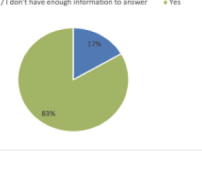
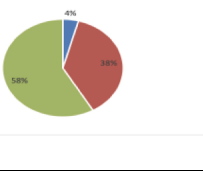
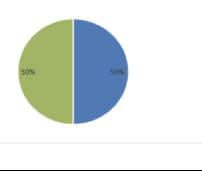
the general population and the prevalence of neuropathic-like pain was seen in 42 % of IA patients versus 6.9 % in the general population when measured using the Douleur Neuropathique (DN4) questionnaire [21]. The presence of small fibre neuropathy in some fibromyalgia patients illustrates the heterogeneity of nociplastic pain [22] and highlights the

importance of developing a suitable outcome measure for nociplastic pain in IA.

Participants from five countries (United States, Denmark, Great Britain, Australia, Canada) including 6 Patient Research Partners (PRP), 2 product makers, 15 Principal Investigator's, 2 providers were

Table 1

Analysis of responses by collaborator groups; all participants and patient research partners response rates are represented in the table.

Poll questions	All Responses	PRP responses and comments out of 6 patient attendees
1. Can patients and clinicians (stakeholders) relate to the term nociplastic pain	Yes: 71% (17) No: 17% (4) Unsure: 12% (3) 	Yes: 4 (67%) No: 1(16%) Unsure:1(17%) 
2. Do you agree that patients with inflammatory arthritis, such as RA, PsA or AxSpA can experience more than one type of pain other than that is caused by inflammation of the joints?	Yes: 100% (24) No: 0% (0) Unsure: 0% (0) 	Yes: 100% No: 0% (0) Unsure: 0% (0) 
3. Can patients consider and report their pain experience if the cause and nature of different types of pain, including nociplastic pain, were explained to them.	Yes: 56% (10) No:11% (2) Unsure:33% (6) Not voted: 6 	Yes: 5 (83%) Unsure:1 (17%) 
4. There is no consensus on which instrument(s) should be used to measure nociplastic pain in inflammatory arthropathy. We are planning a scoping review to identify an instrument or items in an instrument that would help develop one such measurement tool for nociplastic pain. Would you agree this work is important to continue in order to improve treatment of pain in IA?	Yes:86% (19) No: 5% (1) Unsure:9% (2) Not voted: 2 	Yes: 5 (83%) Unsure: 1(17%) 
5. Do you think how nociplastic pain is defined and assessed may need to be modified in the patients with inflammatory arthritis?	Yes 58% (14) No 4% (1) Unsure:38% (9) 	Yes: 3(50%) Unsure: 3(50%) 

Box 1**Nociplastic pain definition and criteria.****NOCIPLASTIC PAIN**

"Pain that arises from altered nociception despite no clear evidence of actual or threatened tissue damage causing the activation of peripheral nociceptors or evidence for disease or lesion of the somatosensory system causing the pain"

Possible nociplastic pain fulfils below conditions

- Report pain of at least 3-month duration
- Report a regional pain distribution
- Report pain that cannot be entirely explained by Nociceptive or Neuropathic mechanisms
- Show clinical signs of pain hypersensitivity phenomenon such as static/dynamic mechanical allodynia, heat or cold allodynia and/or painful after sensations (after the evoked assessments) present in the region of pain.

Probable nociplastic pain in addition fulfils

- history of pain hypersensitivity
- at least one comorbidity: increased sensitivity to light/sound/odours, disturbed sleep, fatigue, or cognitive problems are said to have "probable" nociplastic pain [8,23]

attendees for the pain SIG session. At the end of the SIG meeting, live polls were conducted along with a specific poll for PRPs. Poll questions and responses are listed in Table 1 and Box 2.

Results

The presented evidence on nociplastic pain in IA and the critical need for validated measurement tools, was actively discussed by pain SIG participants. The group emphasized the significance of pain preceding IA diagnosis, suggesting that early pain may increase susceptibility in some patients, underscoring the importance of establishing baseline pain at diagnosis and fostering collaboration with research groups studying pain before disease onset. The heterogeneity of nociplastic pain further highlighted the necessity of capturing individual patient experiences in their own voices which was emphasised by the patients at this session. Participants agreed that as personalised pain medicine advances, integrating patient perspectives and developing quantitative pain assessment tools will be vital for tailoring individualised pain management strategies.

A lively discussion among the workshop attendees focused on the PRP experience which included better patient and clinician communication, attention to the overall pain experience apart from inflammatory joint pain, improvement in pain scoring systems for patients to communicate pain with special emphasis on pain in childhood, pain experience in children from the child and carer perspective, use of pain descriptors, for example the McGill Pain Questionnaire [24]. Other discussion points included a need for careful clinical assessment of standalone primary pain conditions such as fibromyalgia versus IA-related concomitant fibromyalgia, and the consideration for tailored treatment with appropriate DMARD's, biologicals or neuropathic/nociplastic pain treatments [25–27]. There were suggestions to consider pre-existing measurement tools outside of usual pain measurement tools such as the NIH toolbox or PROMIS tool bank [28].

All pain workshop participants agreed there are different and distinguishable pain subtypes experienced in RA, PsA and AxSpA other than the pain of joint inflammation. They also agreed it was important to measure each pain subtype independently with bespoke validated instruments (Table 1). The majority of PRPs (83 % $n = 5/6$) would consider and report their pain experience if the cause and nature of different types of pain, including nociplastic pain, were explained to them (Question 3 Table 1).

>70 % (17/24) of the participants were able to relate to the term nociplastic pain after the informative pain update session although a third of the participants remained uncertain (Question 1 Table 1).

Amongst the PRP attendees, 50 % (3/6) remained unsure or felt they did not have enough information about nociplastic pain phenotype in the context of IA (Question 5 Table 1). There was consensus (Q4 Table 1: 86 % or 19/24) for proceeding with a scoping review to identify relevant instruments or items in an instrument that would help develop a measurement tool for nociplastic pain.

Discussion

The role of unmeasured nociplastic pain was considered by the pain SIG, particularly its potential to modify treatment effects in trials and to confound observational studies and outcome assessments across IA. Only one participant (1/24) thought that the IASP definition and criteria of nociplastic pain can be applied in IA without modifications whereas 96 % (23/24) participants were unsure or suggested these may require contextualisation in patients with IA. This may reflect the novelty of nociplastic pain as a mechanistic pain subtype and there may be a general lack of information to patient groups regarding nociplastic pain. While there was general acceptance of the term nociplastic pain in the context of IA additional suggestions to add footnotes to the existing and accepted nociplastic pain definition [8,11] while framing the limitations of this mechanistic pain subtype within the context of IA pain were discussed. This will allow the OMERACT pain community to address the other important issues such as the development of measurement tools for specific pain subtypes of IA, including nociplastic pain.

The dominant mechanism in nociplastic pain conditions is thought to be central sensitisation although peripheral sensitisation may also play a role [10]. The phenomenon of central sensitisation is well documented in IA [29,30] with outcome measures such as Pain Detect Questionnaire, Central Sensitisation Inventory included in various rheumatological clinical trials to identify presence of concomitant fibromyalgia or central sensitisation alongside the IA condition (Fig. 1) [31–33].

Central sensitisation is defined as "an amplification of neural signalling within the central nervous system that elicits pain hypersensitivity" [23]. This is often demonstrable as lowered pressure pain threshold in musculoskeletal pain conditions including IA [29] and described as evoked pain hypersensitivity in the IASP clinical criteria for nociplastic pain [8]. The presence of central sensitisation symptoms predicts poorer clinical outcomes in IA [6,7,14]. The concept of central sensitisation encourages clinicians to think beyond muscles and joints being pain generators in IA and acknowledge the role of the central nervous system in pain modulation. Developing a measurement tool for nociplastic pain accommodates a shift of focus from assuming pain is solely due to inflammation and towards a normalisation of central nervous system functioning approach that encompasses identification and management of nociplastic pain mechanisms which will facilitate achieving the treat-to-target goals in IA.

The strength of the pain SIG data is inclusion of views of PRP throughout the process incorporating patient perspective (MC) in developing and refining the scoping review protocol which helps to ensure that the outcomes assessed remain relevant to patients. Additionally, presence of diverse and international experts and PRP at the pain SIG supports a broader applicability of the developed measures. However, only a quarter of the SIG participants were PRP and this limits the impact of patient perspective.

The poll results and the SIG participant discussions will inform the next steps for the OMERACT Pain Working Group. Publication of the

Box 2

Results of each poll question.

1. Can patients and clinicians (stakeholders) relate to the term nociplastic pain?

ALL: Majority (> 70 %) were able to relate to the term nociplastic pain after the pain update session although a small proportion continued to remain uncertain or unable to relate to this pain subtype.

PRP: four of the six patient partners found the term relatable, 1 PRP was unsure while one did not find it relatable

2. Do you agree that patients with inflammatory arthritis, such as RA, PsA or AxSpA can experience more than one type of pain other than that is caused by inflammation of the joints? All 24 attendees including PRP's (100 %) agreed there are different and distinguishable pain types experienced in IA separate from pain of joint inflammation. They also agreed it was important to measure each pain subtype

3. Can patients consider and report their pain experience if the cause and nature of different types of pain, including nociplastic pain, were explained to them?

ALL: Although this question was intended for patient partners other attendees also responded to it and therefore the question could not be included as a valid query and rewording of the question was recommended if included in future polls.

Five of the 6 patient partners patient partners responded as affirmative (83 %) while one PRP was unsure

4. There is no consensus on which instrument(s) should be used to measure nociplastic pain in inflammatory arthropathy. We are planning a scoping review to identify an instrument or items in an instrument that would help develop one such measurement tool for nociplastic pain. Would you agree this work is important to continue in order to improve treatment of pain in IA?

A consensus was achieved within a multidisciplinary group (86 %) that included patient partners to continue working towards a scoping review and development of a measurement tool for nociplastic pain.

PRP: Five PRP (83 %) agreed while one remained unsure.

5. Do you think how nociplastic pain is defined and assessed may need to be modified in the patients with inflammatory arthritis?

ALL: Polls revealed a general lack of acceptance of the IASP defined domain - nociplastic pain (58 %). This was an important discussion point among attendees. It was suggested that the nociplastic pain definition and criteria may need to be contextualised to reflect IA conditions.

PRP: within the PRP attendees 50 % remained unsure or felt they did not have enough information. This may reflect the novelty of nociplastic pain as a pain subtype. There may be lack of information to patient groups regarding this pain subtype and implications for patients in terms of assessment of pain and its treatment.

scoping review protocol as preprint on the OSF and presentation of the proposed methodology to review outcome measures for nociplastic pain in IA was an important first step in this process. The highlights of a scoping review protocol developed by the Pain Working Group [12] were presented and discussed at the OMERACT 2025 Pain SIG meeting. A preliminary review of the collated literature for the scoping review to assess candidate instruments for nociplastic pain assessment in IA suggests there may be no off-the-shelf validated tool available to detect the presence of nociplastic pain as per the defined criteria [8].

The responses to polling questions and the pertinent discussion points raised by PRPs and other participants in this meeting strongly support the development of a scoping review to identify outcome measures for nociplastic pain in IA. The proposal to proceed to a fuller scoping review received greater than 70 percent consensus at the OMERACT 2025 SIG pain meeting. The Pain Working Group will continue to develop this important area and report progress to OMERACT.

Collaborative working between the OMERACT Pain Working Group members and the IASP would be helpful to support the development a validated tool to measure nociplastic pain specifically in the context of Inflammatory Arthropathies.

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Ethical statement

This work summarizes outcomes from a structured conference session. No individual-level data were collected, and no identifiable information is reported. Formal ethics approval and written informed consent were not required.

Human and animal rights and informed consent

This article does not contain any studies with human, or animal subjects performed by any of the authors.

CRediT authorship contribution statement

Sharmila Khot: Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Mary Cowern:** Writing – review & editing, Validation, Supervision, Methodology, Conceptualization. **Chris Djurtoft:** Writing – review & editing, Writing – original draft, Visualization, Validation, Methodology. **Robin Christensen:** Writing – review & editing, Writing – original draft, Validation, Supervision, Methodology, Conceptualization. **Philip Mease:** Writing – review & editing, Writing – original draft, Validation, Supervision, Project administration, Methodology, Investigation, Conceptualization. **Lee S Simon:** Writing – review & editing, Resources, Project administration, Methodology, Investigation, Funding acquisition, Formal analysis, Conceptualization. **Ernest Choy:** Writing – review & editing, Supervision, Methodology, Conceptualization.

Declaration of competing interest

The authors declare the following financial interests/personal relationships which may be considered as potential competing interests:

Philip Mease reports a relationship with AbbVie Inc that includes: consulting or advisory, funding grants, and speaking and lecture fees. Philip Mease reports a relationship with Amgen Inc that includes: consulting or advisory, funding grants, and speaking and lecture fees. Philip Mease reports a relationship with ACELYRIN Inc that includes: consulting or advisory. Philip Mease reports a relationship with Bristol-Myers Squibb Company that includes: consulting or advisory and funding grants. Philip Mease reports a relationship with Century that includes: consulting or advisory. Philip Mease reports a relationship with Cullinan Biotech that includes: consulting or advisory. Philip Mease reports a relationship with Eli Lilly that includes: consulting or advisory, funding grants, and speaking and lecture fees. Philip Mease reports a relationship with Genascent that includes: board membership. Philip Mease reports a relationship with Imogene that includes: consulting or advisory. Philip Mease reports a relationship with Johnson & Johnson that includes: consulting or advisory, funding grants, and speaking and lecture fees. Philip Mease reports a relationship with Moonlake that includes: consulting or advisory and funding grants. Philip Mease reports a relationship with Novartis that includes: consulting or advisory and funding grants. Philip Mease reports a relationship with Pfizer that includes: consulting or advisory. Philip Mease reports a relationship with Takeda that includes: consulting or advisory and funding grants. Philip Mease reports a relationship with UCB that includes: consulting or advisory, funding grants, and speaking and lecture fees. If there are

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